

Health Care Optimization

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Hepatitis C in Consumers with Mental illness

Introduction: Approximately 4 million Americans are infected with Hepatitis C. Complicating this is the fact that less than 50 percent know they are infected. A majority of those infected develop chronic infection and can potentially spread the disease to others. While many consumers remain without symptoms, a moderate number progress to end-stage cirrhosis within 10 to 30 years and some of these develop liver cancer, known as hepatocellular carcinoma. As a result, HCV is the leading cause of liver transplantation in the US.

Of particular concern is that HCV infection is 11 times higher in populations with serious mental illness (SMI). One study found that 20.3 percent of adult inpatients in a state psychiatric hospital had positive blood tests for HCV (compared to 1.5 percent in the general population). Part of the reason that Hepatitis C infection rates are so high in consumers with mental illness is tied to behaviors that place them at increased risk for contracting the disease, specifically intravenous (IV) drug use.

The infection rate is even higher in African Americans and Latinos as compared to Caucasians. Unlike Hepatitis A and B, no vaccine is available to prevent HCV.

<u>Point to Case Manager 1:</u> Due to high-risk behaviors, consumers with mental illness are at an increased risk for contracting Hepatitis C. Because Hepatitis C is associated with severe complications in the future, every consumer with mental illness should be screened for Hepatitis C infection with a Hepatitis C antibody test.

The case manager treating mentally ill consumers should be familiar with: (1) Risk factors associated with Hepatitis C infection, (2) blood tests to order to diagnose Hepatitis C, (3) referral of consumers with Hepatitis C to a specialty liver clinic, (4) psychiatric side effects of the medications used to control Hepatitis C infection, especially interferon, (5) special considerations for the consumer with mental illness.

(1) Risk factors associated with Hepatitis C infection.

HCV is primarily spread through infected blood and is often a consequence of IV drug abuse (60 percent of infection in the US is attributable to IV drug use). Therefore substance abuse, especially IV drug abuse and crack cocaine use constitutes the biggest risk factor. Other risk factors associated with HCV include homelessness and experience with jail and prison. In contrast to HIV, transmission of HCV via sexual contact is comparatively low (15 percent of cases attributable to sexual transmission). High-risk sexual behaviors such as multiple partners, unprotected sex and the exchange of sex for drugs or money are associated with

increased rates of HCV infection. These behaviors are known to be higher in consumers with mental illness.

<u>Point to Case Manager 2:</u> As opposed to HIV infection, infection with HCV is not as easily spread sexually. It is predominantly spread by IV drug abuse.

Mental illness also appears to be a risk factor for HCV, although less of one compared to homelessness. The factors relevant to HCV infection are most likely related to high-risk behaviors as opposed to psychiatric impairment. In one study, the rates of HCV in a "soup kitchen" (homeless) population was double that of a comparison population with mental illness (40 percent versus 19 percent). The lifetime use of IV drug use was significantly higher in the homeless group compared to the mental illness group, while a history of risky sexual behavior was similar in both groups. Substance abuse is highly prevalent in both the mentally ill and homeless population. One half of consumers with mental illness meet lifetime criteria for a substance abuse disorder.

Who should be screened for HCV?

Given the high frequency of HCV infection and very high presence of risk factors in the mentally ill population, experts recommend that all consumers with mental illness be screened. Anyone who is HIV positive should also be screened. It is also recommended that consumers also be screened for Hepatitis A and B. Subjects with both Hepatitis B and HCV are more likely to develop severe liver damage and cirrhosis. If the consumer is negative for Hepatitis A and B, they should be provided the vaccines for both infections (i.e., TwinRx injection series).

<u>Point to Case Manager 3:</u> All mentally ill consumers should be screened for HCV infection with Hepatitis C antibody test. If they are positive, they should also be screened for HIV, Hepatitis A and Hepatitis B infections. If consumers are negative for Hepatitis A and B they should be vaccinated for both of these.

(2) Symptoms and course of the infection.

An estimated 60-85 percent of consumers acutely (recently) infected with HCV become chronic carriers. Most who are acutely infected will have a relatively mild disease with slow progression and no symptoms. About one third will develop some constitutional symptoms (nausea, loss of appetite, weakness, weight loss, muscle aches and joint aches) or jaundice. Several of these symptoms can overlap with primary symptoms of coexisting psychiatric disorders, especially depression.

The symptoms of chronic HCV infection do not reflect disease activity, i.e. symptoms do not become worse as the infection progresses. Studies have demonstrated that the above noted symptoms do become more apparent as cirrhosis develops. The symptoms that develop once cirrhosis occurs are much more indicative of the liver damage than infection with HCV.

Without treatment, approximately 20 percent of HCV infected individuals will develop cirrhosis and/or liver cancer in the first 20-30 years after infection. If the HVC infected person's immune system is compromised, such as occurs with co-infection with HIV, the course of HCV is significantly altered with the development of cirrhosis occurring even more frequently (33 percent compared to 11 percent of consumers).

<u>Point to Case Manager 4:</u> Consumers with acute HCV infection may not experience any symptoms and if they do, some of these symptoms may be similar to symptoms experienced as a result of their psychiatric illness. Consumers with chronic HCV infection experience symptoms more frequently and these symptoms are often a reflection of the liver disease rather than the HCV infection itself.

(3) Management of Hepatitis C infection

Not all HCV patients are treated with medication. A liver specialist, known as a hepatologist, experienced in the treatment of HCV will make this determination after additional tests. Two tests often done include: (1) a blood test known that determines the HCV genotype and (2) a liver biopsy. There are 6 types of Hepatitis C viruses (known as genotypes 1 through 6). The different types are defined by specific genotypes (which can be determined by a blood test). It is important to know which specific type of HCV a consumer is infected with because some types respond very well to medications, while others do not. Liver function blood tests, known as transaminases (ALT), are poor indicators of the extent of liver damage.

<u>Point to Case Manager 5:</u> A consumer found to be HCV positive and who is being considered for treatment will need to have HCV genotyping and a liver biopsy done. These two procedures will often determine the best course of treatment.

If treatment is recommended, it usually consists of pegylated (long acting) interferon-alpha (used as an injection beneath the skin) in combination with ribavirin (an oral medication). Treatment length is variable (24 – 48 weeks) and depends primarily on the viral genotype. The goal of treatment is cure, otherwise described as sustained viral response (SVR). Combination treatment can result in sustained virologic response (absence of detectable virus 24 weeks after treatment cessation) in about 50 percent of consumers. For those who achieve SVR, more than 95 percent will remain free of HCV in 10 years. Once treatment is initiated, two blood tests often done include: (1) a viral load and (2) liver function tests. The goal of treatment can be determined by these two blood tests, in terms of: (1) an undetectable viral load and (2) normal liver function tests.

<u>Point to Case Manager 6:</u> The goal of treatment is cure. This is monitored by obtaining blood tests to measure viral load and liver function tests.

In addition to the treatments described above, it is recommended that all consumers with HCV infection discontinue use of alcohol. Continued alcohol use is associated with erratic behavior (continued risky behavior, poor adherence to treatment, secondary depression, suicidal behavior, etc.) and problems with self-care. Alcohol worsens hepatic injury and speeds up progression to cirrhosis and liver cancer. Such consumers should also be advised to avoid other medications that may cause injury to a susceptible liver, such as Tylenol.

If cirrhosis secondary to HCV occurs, adjustment or careful monitoring of psychotropic medications is required. Medications metabolized by the liver, such as clozapine or olanzapine, may need to be reduced. Medications such as valproate, carbamazapine, or nefazedone that have potential to cause liver toxicity on their own should be used with caution (more frequent monitoring of liver function tests).

<u>Point to Case Manager 7:</u> Mentally ill consumers that are HCV positive must be counseled on discontinuing alcohol consumption. Adjustment or careful monitoring of psychotropic medications is also required.

(4) Psychiatric side effects of the medications used to control Hepatitis C infection

Aside from flu-like symptoms (fevers, chills, muscle aches), there are very little other physical side effects with interferon treatment. However, treatment with interferon is associated with a number of psychiatric symptoms:

- Apathy
- Cognitive changes
- Irritability and emotional lability
- Depression
- Suicidal thoughts and, occasionally, completed suicide
- Somatic symptoms including abdominal and joint pain
- Mania has been reported in a few cases

Such symptoms can exacerbate already existing psychiatric symptoms in individuals with mental illness.

<u>Point to Case Manager 8:</u> There are both physical and psychological side effects associated with interferon treatment. The psychiatric side effects are more common and more pronounced. Any mentally ill consumer being started on interferon should be monitored carefully and screened for such side effects.

Depression associated with interferon.

Depression associated with interferon treatment develops in 20-40 percent of consumers. It is characterized by symptoms similar to major depression i.e. depressed mood, irritability, emotional lability, agitation, fatigue, apathy, anhedonia (lack of pleasure), anorexia, psychomotor retardation (slow movement), sleep disturbance, sexual dysfunction, memory impairment, and poor concentration. Depression typically occurs within the first 12 weeks of interferon treatment, but can develop at anytime. Depression can develop rapidly, over a two-week period and usually improves within 2-4 weeks after discontinuation.

How can the risk of depression be managed?

As many as 25 percent of HCV consumers have depressive symptoms even prior to starting interferon. Treatment of pre-existing depression should occur prior to interferon treatment. Some experts argue that uncontrolled depression is a contraindication to treatment with interferon.

A psychiatric evaluation is recommended in high-risk consumers prior to HCV treatment. High risk is defined as:

- Past or current history of depression
- Past psychiatric history or psychiatric hospitalization
- History of suicide attempt
- History of substance abuse
- Family history of affective disorder or suicide

Psychiatric symptoms can sometimes result in discontinuation of interferon treatment, thus aggressive management of depression is recommended for high-risk consumers. It should be noted that the overwhelming majority of mentally ill HCV patients will be "high-risk". For such consumers, the following are recommended:

- Careful monitoring is recommended through an active therapeutic relationship at least every 2 weeks through week 16 of treatment. Monitoring should include assessment of mood symptoms, suicidal ideation, substance use, adherence to treatment, and a mental status exam. If consumer becomes symptomatic, monitoring should be increased to every week.
- Beginning prophylactic treatment with a Selective Seratonin Reuptake Inhibitor (SSRI) antidepressant (such as prozac, zoloft, paxil)

What happens if depression develops in a consumer treated with interferon?

The two primary options available are treatment with an antidepressant or dose reduction of interferon (and occasionally discontinuation of interferon). There are no studies conducted with interferon induced depression. Case reports suggest that SSRIs are effective and can be used safely in these consumers. There is little experience with other antidepressants. The goal of treatment is to allow a consumer to complete the prescribed course of interferon treatment. If severe depression develops that is not responsive to antidepressant medication or results in severe suicidal ideation, discontinuation of interferon is recommended. Questions remain to re-challenging a consumer with interferon once the depression has remitted.

<u>Point to Case Manager 9:</u> Because many consumers with HCV will also have symptoms of depression, it is recommended that all consumers who are about to start interferon treatment be screened for depression. If depression exists it should be aggressively treated prior to interferon administration, or the use of interferon should be reconsidered.

A number of instruments have been developed to assess depression in clinical populations. One especially brief assessment which was designed to specifically measure depression in mentally ill consumers is the Calgary Depression Scale. It is critical that consumers undergoing interferon treatment be assessed for suicidal ideation at every visit.

<u>Point to Case Manager 10:</u> Mentally ill consumers being started on interferon should be monitored closely for the development of depressive symptoms. If this occurs, treatment of the depression with an SSRI should be considered or the interferon should be reduced or withdrawn.

(5) Special considerations for the consumer with mental illness

Knowledge by itself does little to produce behavioral change. Therefore multidimensional treatment is necessary. Substance abuse treatment is critical as this represents a significant risk factor. Ideally, substance abuse and mental health treatment should be integrated. Mentally ill consumers who are HCV positive are less likely to have regular general medical care than those without HCV. Medical and psychiatric care should be coordinated to the extent possible. Under this model non-adherence with treatment and rehabilitation plans that frequently impedes successful treatment can be minimized.

While psychiatric symptoms are often associated with HCV and interferon treatment, they should not be a reason to withhold treatment from psychiatric consumers. Very often medical clinics treating consumers with HCV infection will exclude anyone with a history of psychiatric illness from receiving interferon treatment, despite the fact that there is no evidence to do so.

<u>Point to Case Manager 11:</u> There is sufficient experience to be reassured that HCV treatment can be successfully implemented in the mentally ill consumer. Thus no mentally ill consumer with HCV should be denied interferon treatment solely on the basis of his/her mental illness.

The following summarizes the main points discussed in this monograph:

- 1. Hepatitis C infection is mainly transmitted by intravenous drug abuse and less so sexually. Due to the fact that several consumers with mental illness may also abuse intravenous drugs, the rates of Hepatitis C infection in consumers with mental illness are much greater than the general population.
- 2. Every consumer with mental illness should be screened for Hepatitis C infection and if positive, should undergo a thorough psychiatric evaluation to determine if they are candidates for interferon treatment.
- 3. If a consumer with mental illness is positive for Hepatitis C, he/she should also be screened for HIV, Hepatitis A and Hepatitis B infections. If consumers are negative for Hepatitis A and B they should be vaccinated for both of these.
- 4. Consumers with Hepatitis C infection may not have any symptoms at all, making it even more difficult to recognize unless you specifically screen for it. Symptoms occur more frequently once the disease becomes chronic and the individual has been living with it for years. At that point, the symptoms that occur are more a reflection of the direct damage the virus has on the liver (i.e. jaundice, fatigue, abdominal pain).
- 5. Any consumer diagnosed with Hepatitis C infection must be referred to a liver specialist to determine the best course of treatment.
- 6. A consumer initially diagnosed with Hepatitis C will require both a liver biopsy and a blood test to specifically determine the Hepatitis C genotype. This information will determine what (if any) treatment the consumer would require.
- 7. Treatment usually consists of interferon alpha (an injection) and/or ribavirin (an oral medication).
- 8. Once treatment is initiated a viral load and liver function tests (both of these are obtained from a blood test) are used to determine response to treatment. The goal of treatment is to cure (undetectable viral load) or to prevent progression of the disease (prevent worsening of the liver function tests).
- 9. Consumers with Hepatitis C infection also need to be counseled to avoid alcohol or any other substances that can cause further damage to their liver.
- 10. Consumers with mental illness who are Hepatitis C positive need to have all their medications reviewed. Psychiatric medications that are cleared from the liver may need to have their dosages adjusted. Psychiatric medications that may cause damage to the liver may need to be monitored much more closely (i.e. more frequent liver function tests) or may need to be eliminated completely.

- 11. There are both physical and psychological side effects associated with interferon treatment. The physical side effects are often flu-like symptoms. The psychiatric side effects are more common and more pronounced. Any mentally ill consumer being started on interferon should be monitored carefully and screened for such side effects.
- 12. Because several consumers with HCV will also have depression, it is recommended that all consumers who are about to start interferon treatment be screened for depression. If depression exists it should be aggressively treated prior to interferon administration, or the use of interferon should be reconsidered.
- 13. Mentally ill consumers being started on interferon should be monitored closely for the development of depressive symptoms. If this occurs, treatment of the depression with an SSRI should be considered or the interferon should be withdrawn.
- 14. No mentally ill consumer with HCV should be denied interferon treatment solely on the basis of his/her mental illness if there is no evidence of severe depression.